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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ZEMAN, ROBERT A	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 09/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/517,491	BERLIN, VIVIAN	
	Examiner	Art Unit	
	Robert A. Zeman	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *51-74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *51-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2-14-05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The response filed on 9-22-2004 is acknowledged. Claims 51-62 have been amended. Claims 62-74 have been added. Claims 51-74 are pending and currently under examination.

Priority

Applicant's comments regarding the claimed priority are acknowledged. The instant application a continuation under 37 CFR 1.53(b) of U.S. Application 08/360,144, filed on December 20, 1994 which is a continuation-in-part (CIP) of U.S. Application 08/250,795, filed on 5-27- 1 994. The instant claims are drawn to antibodies that bind to either a murine or human RAPTI protein comprising the sequence of SEQ ID NO:2 or SEQ ID NO:12, respectively. Said antibodies also do not substantially cross-react with a fungal TOR1 or TOR2 protein. However, since U.S. Application 08/250,795 does not disclose the sequences set forth in SEQ ID NO:2 or SEQ ID NO:12 nor does it disclose antibodies that specifically bind to a RAPTI protein and do not substantially cross react with a fungal TORI or TOR2 protein, the filing date of the application 08/360,144 (12-20-1994) will be used with regard to the availability of prior art under 35 U.S.C. 1 02.

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. [1] as follows:

A reference to the prior application must be inserted as the first sentence(s) of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e), 120, 121, or

365(c). See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, 121, or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) and current status of all nonprovisional applications.

Information Disclosure Statement

The Information Disclosure statement filed on 2-14-2005 has been considered. An initialed copy is attached hereto.

Claim Rejections Withdrawn

The rejection of claims 51-62 under 35 U.S.C. 103(a) as being unpatentable over Sabatini et al. (Cell Vol. 78, pages 35-43, July 15, 1994) in view of Campbell (Monoclonal Antibody Technology, Elsevier, N.Y. 1984; chapter 1, pages 1-32) is withdrawn. Sabatini et al. does not disclose a sequence that is identical to that set forth in SEQ ID NO:2

Claim Rejections Maintained and New Grounds of Rejection

USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 51-74 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons set forth in the previous Office action in the

rejection of claims 51-62. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a vast genus of antibodies, which bind to a murine or human RAPT1 protein wherein said RAPT1 protein includes a FKBP/rapamycin binding domain that binds to a FKBP/rapamycin complex. To fulfill the written description requirements set forth under 35 USC § 112, first paragraph, the specification must describe at least a substantial number of the members of the claimed genus, or alternatively describe a representative member of the claimed genus, which shares a particularly defining feature common to at least a substantial number of the members of the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as to reasonably convey to the skilled artisan that Applicant has possession the claimed invention. To adequately describe the genus of antibodies, Applicant must adequately describe the proteins encompassed by claim 1 to which the antibodies bind. That description must include a description of the FKBP/rapamycin binding domains and the FKBP/rapamycin complexes encompassed by claim 1. However, the specification does not disclose distinguishing and identifying features of a representative number of members of the genus of proteins to which the claims are drawn, such as a correlation between the structure of the protein (and FKBP/rapamycin binding domains) and its recited function, so that the skilled artisan could immediately envision, or recognize at least a substantial number of members of the claimed genus of antibodies. Moreover, the specification fails to disclose which amino acid residues are essential to the function of the protein, or which amino acids might be added, replaced or deleted so that the resultant peptide

retains the activity of its parent, or by which other amino acids the essential amino acids might be replaced so that the resultant peptide retains the activity of its parent. Therefore, the specification fails to adequately describe at least a substantial number of members of the genus of proteins to which the claims refer; and accordingly the specification fails to adequately describe at least a substantial number of members of the claimed genus of antibodies.

MPEP § 2163.02 states, "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided:

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the "written description" inquiry, *whatever is now claimed.*

See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, "Written Description" Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing

distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed.

The *Guidelines* further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. As evidenced by the teachings of Skolnick et al., the art is unpredictable. Skolnick et al. (*Trends in Biotechnology* **18**: 34-39, 2000) discloses the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (see, e.g., the abstract; and page 34, *Sequence-based approaches to function prediction*). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the

structurally related protein (see, in particular, the abstract and Box 2). Thus, one skilled in the art would not accept the assertion, which is based only upon an observed similarity in amino acid sequence, that a variant of the polypeptide of SEQ ID NO:2 or SEQ ID NO:12 is a murine or human RAPT1 protein includes a FKBP/rapamycin binding domain that binds to a FKBP/rapamycin complex. Therefore, because the art is unpredictable, in accordance with the *Guidelines*, the description of claimed antibodies is not deemed representative of the genus of peptides to which the claims refer.

Finally it should be noted that the courts have recently decided in Randolph J. Noelle v Seth Lederman, Leonard Chess and Michael J. Yellin (CAFC, 02-1187, 1/20/2004) that:

> a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. See Enzo Biochem II, 323 F.3d at 965; Regents, 119 F.3d at 1568. Therefore, based on our past precedent, as long as an applicant has disclosed a "fully characterized antigen," either by its structure, formula, chemical name, or physical properties, or by depositing the protein in a public depository, the applicant can then claim an antibody by its binding affinity to that described antigen.
>
> Noelle did not provide sufficient support for the claims to the human CD40CR antibody in his '480 application because Noelle failed to disclose the structural elements of human CD40CR antibody or antigen in his earlier '799 application. Noelle argues that because antibodies are defined by their binding affinity to antigens, not their physical structure, he sufficiently described human CD40CR antibody by stating that it binds to human CD40CR antigen. Noelle cites Enzo Biochem II for this proposition. This argument fails, however, because Noelle did not sufficiently describe the human CD40CR antigen at the time of the filing of the '799 patent application. In fact, Noelle only described the mouse antigen when he claimed the mouse, human, and genus forms of CD40CR antibodies by citing to the ATCC number of the hybridoma secreting the mouse CD40CR antibody. If Noelle had sufficiently described the human form of CD40CR antigen, he could have claimed its antibody by simply stating its binding affinity for the "fully characterized" antigen. Noelle did not describe human CD40CR antigen. Therefore, Noelle attempted to define an unknown by its binding affinity to another unknown. As a result, Noelle's claims to human forms of CD40CR antibody found in his '480 application cannot gain the benefit of the earlier filing date of his '799 patent application.
>
> Moreover, Noelle cannot claim the genus form of CD40CR antibody by simply describing mouse CD40CR antigen.

Applicant argues that the amendment to the instant claims renders the rejection moot. However, since Applicant has not fully characterized the protein to which the claimed antibodies bind (including the FKBP/rapamycin binding domains and FKBP/rapamycin complexes encompassed by said claims) the written description requirements under 35 U.S.C 112, first paragraph have not been met.

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 51-54 and 63-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sabatini et al. (Cell Vol. 78, pages 35-43, July 15, 1994) in view of Campbell (Monoclonal Antibody Technology, Elsevier, N.Y. 1984; chapter 1, pages 1-32).

Applicant argues:

1. Since the instant application claims priority to US Application 08/250,795 filed on May 27, 1994, Sabatini et al. is not available as art.

Applicant's arguments have been fully considered and deemed non-persuasive. As explained above, , since U.S. Application 08/250,795 does not disclose the sequences set forth in SEQ ID NO:2 or SEQ ID NO:12 nor does it disclose antibodies that specifically bind to a RAPTI protein and do not substantially cross react with a fungal TORI or TOR2 protein, the filing date of the application 08/360,144 (12-20-1994) will be used with regard to the availability of prior art under 35 U.S.C. 1 02.

Sabatini et al. disclose the amino acid sequence for mammalian RAFT1 that fully incorporates 12 of the instant application (see Figure 5 and STIC search printout, attached). Sabatini et al differ from the instant invention in that they do not disclose antibody preparations (either monoclonal or polyclonal) that are specifically immunoreactive with a mammalian RAPT1 protein and do not substantially cross react (binding affinity of less than 10 percent) with a fungal TOR1 or TOR2 protein or antibodies that are specifically immunoreactive with a RAPT1 protein having an amino acid sequence that is identical to SEQ ID NO:12 of the instant application. Campbell discloses that "It is customary now for any group working on a macromolecule to both clone the genes coding for it and make monoclonal antibodies to it (sometimes without a clear objective for their application)"[see page 29]. Consequently, it would have been obvious to one of skill in the art to make antibodies to the proteins disclosed by Sabatini et al. Moreover, since SEQ ID NO:12 codes for the biologically active region of the RAFT1 protein disclosed by Sabatini et al., any antibodies raised against said RAFT1 protein

would bind (i.e. immunoreact) with a protein having a sequence set forth in either SEQ ID NO:12. With regard to the new added limitations, the RAPT1 proteins encompassed by SEQ ID NO: 12, necessarily contain FKBP/rapamycin binding domain since they have been disclosed to have the ability to bind FKBP/rapamycin complex (see pages 18-19 of the specification).

Claims 63-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (Nature Vol. 369, pages 756-758, June 30, 1994) in view of Campbell (Monoclonal Antibody Technology, Elsevier, N.Y. 1984; chapter 1, pages 1-32) for the reasons set forth in the previous Office action in the rejection of claims 51-62.

Applicant argues:

1. Since the instant application claims priority to US Application 08/250,795 filed on May 27, 1994, Brown et al. is not available as art.

Applicant's arguments have been fully considered and deemed non-persuasive.. As explained above, since U.S. Application 08/250,795 does not disclose the sequences set forth in SEQ ID NO:2 or SEQ ID NO:12 nor does it disclose antibodies that specifically bind to a RAPTI protein and do not substantially cross react with a fungal TORI or TOR2 protein, the filing date of the application 08/360,144 (12-20-1994) will be used with regard to the availability of prior art under 35 U.S.C. 102.

Therefore, as outlined previously, Brown et al. disclose the amino acid sequence for human FRAP which fully incorporates SEQ ID NO :2 and 12 of the instant application (see page 757 and STIC search printout, attached). Brown et al. differs from the instant invention in that they do not disclose antibody preparations (either monoclonal or polyclonal) that are specifically

immunoreactive with a human FRAP protein and do not substantially cross react (binding affinity of less than 10 percent) with a fungal TOR1 or TOR2 protein or antibodies that are specifically immunoreactive with a RAPT1 protein having an amino acid sequence of either SEQ ID NO:2 or 12 of the instant application. Campbell discloses that "It is customary now for any group working on a macromolecule to both clone the genes coding for it and make monoclonal antibodies to it (sometimes without a clear objective for their application)"[see page 29]. Consequently, it would have been obvious to one of skill in the art to make antibodies to the proteins disclosed by Brown et al. Moreover, since SEQ ID NO:2 and 12 code for the biologically active region of the RAFT1 protein disclosed by Brown et al., any antibodies raised against said RAFT1 protein would necessarily bind with a protein with the sequence set forth in SEQ ID NO:2 and 12. With regard to the new added limitations, the RAPT1 proteins encompassed by SEQ ID NO:2 and 12, necessarily contain FKBP/rapamycin binding domain since they have been disclosed to have the ability to bind FKBP/rapamycin complex (see pages 18-19 of the specification).

New Grounds of Rejection

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 51-74 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 33 of copending Application No. 10/877,320. Although the conflicting claims are not identical, they are not patentably distinct from each other because both claim sets are drawn to antibodies that bind to RAPT1 proteins with the sequence of SEQ ID NO:2 or 12 (i.e. murine or human RAPT1).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (571) 272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ROBERT A. ZEMAN
PATENT EXAMINER
September 22, 2005